

HEART

Editorial

Atrial fibrillation begets trouble

Atrial fibrillation is the most common sustained cardiac arrhythmia. The disorder has been known for over a hundred years, and is regarded by many as an acceptable alternative to sinus rhythm. This is unlikely to be correct; atrial fibrillation leads to thromboembolism, poor quality of life, and impaired left ventricular function. The false perception arises because the symptomatic impact of atrial fibrillation can be subtle and non-specific, and the deleterious effects occur insidiously or as events remote from the time of onset of the arrhythmia. In these regards, atrial fibrillation is better compared to disorders such as hypertension rather than ventricular tachycardia or acute coronary syndromes. As four-fifths of patients with permanent atrial fibrillation and half of those with the paroxysmal form have other cardiovascular disease, it is difficult to determine which symptoms are due to atrial fibrillation and which stem from the underlying disease.

The importance of atrial fibrillation as a cause of stroke and other thromboembolic complications is well documented. Data from the Framingham Study¹ have shown that atrial fibrillation emerges in multivariate analysis as an independent risk factor for stroke (risk ratio 5.6 compared with matched controls in sinus rhythm). The risk from atrial fibrillation is even higher in patients with hypertension (risk ratio 12),² heart failure (12)² or mitral stenosis (17).¹ Prospective trials have shown a reduction in risk by two-thirds if patients are adequately anticoagulated.³ Unfortunately, low intensity anticoagulation (INR 1.2-1.5), even combined with aspirin, is not as good as full anticoagulation (INR 2-3).⁴ This was recently confirmed by the case control study of strokes in patients on anticoagulants from Hylek *et al*⁵ that showed the risk of stroke rose steeply as the INR fell progressively from a value of 2. Others have demonstrated that haemorrhagic risk increases rapidly after the INR exceeds 4, but is low below INR values of 3.⁶ Taken together, these data suggest that with ideal anticoagulation (INR constantly maintained between 2 and 3) it may be possible to counter totally the thromboembolic risk which results from atrial fibrillation. Unfortunately, precise anticoagulant control is not always possible, and anticoagulation is contraindicated in many patients. Moreover, anticoagulation in atrial fibrillation is a lifelong undertaking and is associated with substantial costs, inconvenience, and restriction of activities. Atrial fibrillation is also associated with silent cerebral infarction⁷⁻⁹ that, in one small series, was not prevented by anticoagulation.⁷ The clinical significance, long term implications for cognitive function, and whether cardioversion or anticoagulation/antiplatelet therapy are preventative remain to be definitively determined.

There are many case reports and short series which describe a reversible ventricular dilated cardiomyopathy induced by atrial fibrillation.¹⁰⁻¹⁴ What causes some patients but not others to develop cardiomyopathy is unknown. Inadequate heart rate control is the prime suspect, and certainly some have documented reversal of cardiomyopathy without restoration of sinus rhythm through

rigorous rate control by AV nodal ablation,¹⁰ or even using drugs which, although negatively dromotropic, are also negatively inotropic.¹¹ Tachycardia cardiomyopathy can also result from regular tachycardias or near incessant paroxysmal tachycardias. It is odd, however, that atrial flutter has very rarely been reported as the culprit arrhythmia, as it often causes a tachycardia of 150 beats/min. This is faster than the resting rate typically seen in atrial fibrillation, and the irregularity of the cardiac rhythm in atrial fibrillation is a possible co-factor to explain this discrepancy. At the same mean heart rate, an irregular rhythm is associated with a lower cardiac output than a regular one,^{15,16} and atrial fibrillation causes relative hypoperfusion of the endocardium as well as increased myocardial oxygen extraction.¹⁷ A possible mechanism for this can be found in the phenomenon of post-extrasystolic potentiation, whereby the beat following a short duration cycle generates more work than the average but is associated with an even higher rise in oxygen consumption and a consequent drop in cardiac efficiency.¹⁸ Many patients with atrial fibrillation have cardiac failure; often no clear independent cause for the failure is documented. In such patients atrial fibrillation should be considered as a potential cause of the heart failure rather than merely a consequence. Attempts at cardioversion or rigorous heart rate control should be undertaken despite the associated presence of heart failure.

It is possible that the long term deleterious effects of atrial fibrillation on left ventricular function may be far more widespread than is currently appreciated. In a prospective study, Van Gelder *et al*¹⁹ found that among patients who remained in sinus rhythm for at least six months following cardioversion, a progressive improvement in left ventricular function and exercise capacity appeared to occur. Recovery of left atrial mechanical function, which is known to be impaired for hours to several weeks following cardioversion²⁰ did not wholly explain these findings, and the authors suggested that the atrial fibrillation may have had a direct effect on left ventricular function despite effective rate control with digoxin and verapamil. The results of this small trial need to be confirmed.

Considering the frequency of atrial fibrillation in the population, the symptomatic impact of the disorder has been little studied. Jenkins *et al*²¹ found quality of life in patients with atrial fibrillation was less than that of patients recovering from myocardial infarction or with severe rheumatoid arthritis, but their patients were about to undergo AV nodal ablation with pacemaker implantation, and were probably drawn from the most symptomatic group. Our own survey and that of others²¹ demonstrate that exertion dyspnoea, lassitude, and lack of energy are the predominant symptoms of atrial fibrillation. Palpitation, which is commonly perceived to be the principal complaint, features far less in the symptoms that patients spontaneously volunteer. The symptoms of atrial fibrillation are non-specific and often attributed to co-exis-

tent disease, but they are very real and often very debilitating. Restoration of sinus rhythm is associated with an improvement in exercise capacity,^{22,23} a finding which contrasts with the effect of pharmacological rate control. A few studies have suggested that drugs improve exercise capacity,^{24,25} but many others have failed to show significant benefit.²⁶⁻²⁸

In addition to the lack of awareness of the adverse effects of atrial fibrillation, the other feature which has encouraged the tacit acceptance of the arrhythmia is the lack of effective therapy. External DC cardioversion can restore sinus rhythm in 70–90% of patients, but atrial fibrillation recurs in the majority within a year. Prophylactic antiarrhythmic drug therapy doubles the number remaining in sinus rhythm,^{29,30} and still higher figures might be achievable through the use of amiodarone³¹ or serial drug therapy.^{32,33} However, proarrhythmia and an increased risk of sudden death are a concern.^{29,34} Further improvements in our ability to restore sinus rhythm have resulted from the development of internal cardioversion (that is, defibrillating with one or both poles within the heart), which has a higher success rate than external cardioversion³⁵ and may be effective in those resistant to external shocks.³⁵⁻³⁷

The duration of atrial fibrillation is one of the best predictors of recurrence following cardioversion, and at least part of the electrophysiological basis for the fact that "atrial fibrillation begets atrial fibrillation" has been demonstrated by Wijffels *et al* in a goat model.³⁸ Atrial fibrillation was repeatedly induced by rapid atrial pacing and, after several days, persistent atrial fibrillation resulted. Changes in the electrophysiological characteristics of the goat atria, which favour the induction and maintenance of atrial fibrillation, were demonstrable and these persisted for a couple of days following cardioversion. In humans, a high risk of recurrence of atrial fibrillation persists for several months following cardioversion, so there must be additional important factors. These data suggest though that prompt restoration of sinus rhythm, both at the initial onset and after recurrences of atrial fibrillation, may be far more important in the long term prognosis of the disorder than has previously been appreciated. This concept has been recently supported by preliminary clinical observations.³⁹

Thus atrial fibrillation causes numerous deleterious effects and is still difficult to treat. Our therapeutic choices are currently expanding but the long term restoration of sinus rhythm can still not be the goal for all. The important principle is to investigate and treat appropriately from the outset to minimise the chances of adverse events and maximise the chances of maintaining sinus rhythm. Without proper treatment, atrial fibrillation begets trouble.

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- Wolf PA, Dawber TR, Thomas HE, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham Study. *Neurology* 1978;28:973-7.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991;22:983-8.
- Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. *Arch Intern Med* 1994;154:1449-57.
- Stroke Prevention in Atrial Fibrillation Investigators. Adjusted-dose warfarin versus low-intensity warfarin plus aspirin for high risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Lancet* 1996;348:633-8.
- Hylek EM, Skates SJ, Sheehan MA, Singer DE. An analysis of the lowest effective intensity of prophylactic anticoagulation for patients with non-rheumatic atrial fibrillation. *N Engl J Med* 1996;340:540-6.
- Cannegieter SC, Rosendaal FR, Wintzen AR, van der Meer FJ, Vandenberghe JP, Briet E. Optimal oral anticoagulant therapy in patients with mechanical heart valves. *N Engl J Med* 1995;333:11-17.
- Ezekowitz MD, James KE, Nazarian SM, Davenport J, Broderick JP, Gupta SR, *et al*. Silent cerebral infarction in patients with nonrheumatic atrial fibrillation. The Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *Circulation* 1995;92:2178-82.
- Petersen P, Madsen EB, Brun B, Pedersen F, Gyldested C, Boysen G. Silent cerebral infarction in chronic atrial fibrillation. *Stroke* 1987;18:1098-100.
- Feinberg WM, Seeger JF, Carmody RF, Anderson DC, Hart RG, Pearce LA. Epidemiologic features of asymptomatic cerebral infarction in patients with nonvalvular atrial fibrillation. *Arch Intern Med* 1990;150:2340-4.
- Rodriguez LM, Smeets JL, Xie B, de Chillou C, Cheriex E, Pieters F, *et al*. Improvement in left ventricular function by ablation of atrioventricular nodal conduction in selected patients with lone atrial fibrillation. *Am J Cardiol* 1993;72:1137-41.
- Van Den Berg MP, van Veldhuisen DJ, Crijns HJ, Lie KI. Reversion of tachycardiomyopathy after beta-blocker [letter]. *Lancet* 1993;341:1667.
- Grogan M, Smith HC, Gersh BJ, Wood DL. Left ventricular dysfunction due to atrial fibrillation in patients initially believed to have idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992;69:1570-3.
- Haïat R, Halphen C, Stoltz JP, Leroy G, Soussana C. [Auricular fibrillation: a cause of reversible myocardiopathy]. [French]. *Ann Cardiol Angeiol* 1987;36:417-19.
- Peters KG, Kienle MG. Severe cardiomyopathy due to chronic rapidly conducted atrial fibrillation: complete recovery after restoration of sinus rhythm. *Am J Med* 1988;85:242-4.
- Daoud E, Weiss R, Bahu M, *et al*. Effect of a regular and irregular rhythm on cardiac output [abstract]. *PACE* 1996;19:691.
- Naito M, David D, Michelson EL, Schaffenburg M, Dreifus LS. The hemodynamic consequences of cardiac arrhythmias: evaluation of the relative roles of abnormal atrioventricular sequencing, irregularity of ventricular rhythm and atrial fibrillation in a canine model. *Am Heart J* 1983;106:284-91.
- Friedman HS, Scorza J, McGuinn R, Shaughnessy E. The effects of atrial fibrillation on myocardial blood flow and energetics. *Proc Soc Exp Biol Med* 1985;180:1-8.
- Geschwind H, Huet Y, Laine JF, Teisseire B, Dhainaut JF, Laurent D. [Energy cost of postextrasystolic potentiation in man]. [French]. *Arch Mal Coeur Vaiss* 1984;77:747-53.
- Van Gelder IC, Crijns HJ, Blanksma PK, Landsman ML, Posma JL, Van Den Berg MP, *et al*. Time course of hemodynamic changes and improvement of exercise tolerance after cardioversion of chronic atrial fibrillation unassociated with cardiac valve disease. *Am J Cardiol* 1993;72:560-6.
- Shapiro EP, Effron MB, Lima S, Ouyang P, Siu CO, Bush D. Transient atrial dysfunction after conversion of chronic atrial fibrillation to sinus rhythm. *Am J Cardiol* 1988;62:1202-7.
- Jenkins LS, Ellenbogen K, Kay N, Giudici M, Jensen N, Martin R, *et al*. Quality of life in patients with symptomatic atrial fibrillation [abstract]. *Circulation* 1995;92(suppl I):490.
- Lipkin DP, Frenneaux MP, Stewart R, Joshi J, Lowe T, McKenna WJ. Delayed improvement in exercise capacity after cardioversion of atrial fibrillation to sinus rhythm. *Br Heart J* 1988;59:572-7.
- Ueshima K, Myers J, Morris CK, Atwood JE, Kawaguchi T, Froelicher VF. The effect of cardioversion on exercise capacity in patients with atrial fibrillation. *Am Heart J* 1993;126:1021-4.
- Lang RM, Klein HO, Weiss E, David D, Sareli P, Levy A, *et al*. Superiority of oral verapamil therapy to digoxin in treatment of chronic atrial fibrillation. *Chest* 1983;83:491-9.
- Pomfret SM, Beasley CR, Challenor V, Holgate ST. Relative efficacy of oral verapamil and digoxin alone and in combination for the treatment of patients with chronic atrial fibrillation. *Clin Sci* 1988;74:351-7.
- Dahlstrom CG, Edvardsson N, Nasheng C, Olsson SB. Effects of diltiazem, propranolol, and their combination in the control of atrial fibrillation. *Clin Cardiol* 1992;15:280-4.
- Lewis RV, Irvine N, McDevitt DG. Relationships between heart rate, exercise tolerance and cardiac output in atrial fibrillation: the effects of treatment with digoxin, verapamil and diltiazem. *Eur Heart J* 1988;9:777-81.
- Atwood JE, Myers JN, Sullivan MJ, Forbes SM, Pewen WF, Froelicher VF. Diltiazem and exercise performance in patients with chronic atrial fibrillation. *Chest* 1988;93:20-5.
- Coplen SE, Antman EM, Berlin JA, Hewitt P, Chalmers TC. Efficacy and safety of quinidine therapy for maintenance of sinus rhythm after cardioversion. A meta-analysis of randomized control trials. *Circulation* 1990;82:1106-16.
- Van Gelder IC, Crijns HJ, Van Gilst WH, Van Wijk LM, Hamer HP, Lie KI. Efficacy and safety of flecainide acetate in the maintenance of sinus rhythm after electrical cardioversion of chronic atrial fibrillation or atrial flutter. *Am J Cardiol* 1989;64:1317-21.
- Gold RL, Haffajee CI, Charos G, Sloan K, Baker S, Alpert JS. Amiodarone for refractory atrial fibrillation. *Am J Cardiol* 1986;57:124-7.
- Crijns HJ, Van Gelder IC, Van Gilst WH, Hillege H, Gosselink ATM, Lie KI. Serial antiarrhythmic drug treatment to maintain sinus rhythm after electrical cardioversion for chronic atrial fibrillation or atrial flutter. *Am J Cardiol* 1991;68:335-41.
- Antman EM, Beamer AD, Cantillon C, McGowan N, Friedman PL. Therapy of refractory symptomatic atrial fibrillation and atrial flutter: a staged care approach with new antiarrhythmic drugs. *J Am Coll Cardiol* 1990;15:698-707.
- Flaker GC, Blackshear JL, McBride R, Kronmal RA, Halperin JL, Hart RG. Antiarrhythmic drug therapy and cardiac mortality in atrial fibrillation. *J Am Coll Cardiol* 1992;20:527-32.
- Levy S, Lauribe P, Dolla E, Kou W, Kadish A, Calkins H, *et al*. A randomized comparison of external and internal cardioversion of chronic atrial fibrillation. *Circulation* 1992;86:1415-20.
- Baker BM, Botteron GW, Smith JM. Low-energy internal cardioversion for atrial fibrillation resistant to external cardioversion. *J Cardiovasc Electrophysiol* 1995;6:44-7.
- Sopher SM, Murgatroyd FDM, Slade AKB, Blankoff I, Ward DE, Rowland E, *et al*. Low energy transvenous cardioversion of atrial fibrillation resistant to transthoracic shocks. *Heart* 1996;75:635-8.
- Wijffels MCEF, Kirchhof CJHJ, Dorland R, Allesie MA. Atrial fibrillation begets atrial fibrillation: A study in awake chronically instrumented goats. *Circulation* 1995;92:1954-68.
- Sulke N, Kamalvand K, Tan K, Smeeton N, Stafford P, Vincent R. A prospective evaluation of recurrent atrial endocardial defibrillation in patients with refractory chronic atrial fibrillation and flutter [abstract]. *Heart* 1996;75(suppl 1):P42.